

## **SECTION 2 NON-TECHNICAL ABSTRACT**

Prostate cancer is the most commonly diagnosed malignancy in men. Although conventional therapies (surgery and radiation therapy) produce high cure rates of early stage prostate cancer, many of these tumors recur and metastasize. Unfortunately, effective therapies are still lacking for recurrent and advanced stages of this disease.

In light of this, we have developed a novel, multi-faceted gene therapy approach for the treatment of prostate cancer. Our approach utilizes a modified cold virus, called an adenovirus, to selectively and efficiently deliver a pair of therapeutic "suicide genes" to prostate tumors. The virus itself generates a potent anti-tumor effect by preferentially replicating in and destroying prostate tumor cells. The tumor-specific killing effect of the virus can be enhanced by combining it with a form of tumor-targeted chemotherapy called suicide gene therapy. Activation of the suicide genes renders malignant cells sensitive to specific pharmacological agents (prodrugs) and sensitizes them to the therapeutic effects of radiation. Importantly, the suicide gene systems can be used to control viral replication, providing a safeguard against excessive viral spread.

In this study, the safety and effectiveness of the combined viral/suicide gene therapy approach will be evaluated in patients with local recurrence of prostate cancer. The virus will be injected into the tumors under ultrasound guidance. Three groups of four patients will be given an increasing dose of the virus, starting with the lowest dose and progressing to the next dose only after the procedure has demonstrated to be safe. Two days after injection of the virus into the tumor, patients will receive two non-toxic drugs, called prodrugs, one orally and the other intravenously, for the next seven days. Patients will be monitored closely and if there are no serious adverse side effects, the next group of four patients will be treated with a higher viral dose. A total of 12 patients will be enrolled. Effectiveness will be monitored by serial measurements of serum prostate specific antigen (PSA), digital rectal exam (DRE), transrectal ultrasound (TRUS) of the prostate, and biopsy of the prostate. The primary objective of this study is to determine whether the treatment is safe for use in humans.